



Fibrotic Sarcoidosis Mimics Non-specific Interstitial Pneumonia: A Case Report

**Tomoo Kishaba^{1*}, Junya Fukuoka², Yuichiro Nei¹, Hiroaki Nagano¹,
Shin Yamashiro¹ and Fumihito Kunishima³**

¹*Department of Respiratory Medicine, Okinawa Chubu Hospital, Miyazato 281, Uruma City, Okinawa, Japan.*

²*Department of Pathology, Nagasaki University Graduate School of Biomedical Sciences, 1-12-4 Sakamoto, Nagasaki-City, Nagasaki, Japan.*

³*Devison of Pathology, Okinawa Chubu Hospital, Miyazato 281, Uruma City, Okinawa, Japan.*

Authors' contributions

This work was carried out in collaboration between all authors. Author TK did the concept and designed the study. Authors HN, SY and YN participated in data collection. Authors TK, JF and HN wrote the manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2017/33805

Editor(s):

- (1) Pietro Scicchitano, Cardiology Department, Hospital "F. Perinei" Altamura (Ba), Italy.
(2) Butov Dmytro, Associate Professor, Vice Head of the Department of Phthisiology and Pulmonology, Kharkiv National Medical University, Kharkiv, Ukraine.

Reviewers:

- (1) Serdar Özkan, MEDOVA Hospital, Turkey.
(2) Laren Tan, Loma Linda University, USA.

Complete Peer review History: <http://www.sciedomains.org/review-history/19305>

Case Study

Received 29th April 2017
Accepted 24th May 2017
Published 2nd June 2017

ABSTRACT

Aims: Fibrotic sarcoidosis is not common presentation and it is not easy to diagnose for many differential diagnosis. We herein report an interesting fibrotic sarcoidosis who shows atypical presentation such as progressive dyspnea with fibrotic imaging findings.

Presentation of Case: A 75-year-old Japanese lady visited our hospital with fifteen months duration of non-productive cough and one month exertional dyspnea. Physical examination revealed bilateral fine crackles and squawk at left lung base. Laboratory findings showed elevation of lactate dehydrogenase (LDH) and Krebs von den Lungen-6 (KL-6). Chest high-resolution computed tomography (HRCT) showed mediastinal lymphadenopathy, left lower lung field dominant reticular shadow and traction bronchiectasis. In terms of pulmonary function test (PFT), percent predicted vital capacity (%VC), forced vital capacity (FVC) and percent predicted forced vital capacity (%FVC) were 71.2%, 1.12L and 52.8%, respectively. Based on clinical course,

*Corresponding author: E-mail: kishabatomo@gmail.com;

laboratory findings and chest imaging, we considered possibility of fibrotic non-specific interstitial pneumonia (f-NSIP). She undertook video-assisted thoracoscopic surgery (VATS). Specimens were taken from left upper lobe and lower lobe. Pathological findings showed well-formed peri-lymphatic granuloma, architectural destruction with dense fibrosis and microscopic honeycombing. According to the clinical-radiological-pathological discussion, we diagnosed this case as fibrotic sarcoidosis. We commenced oral prednisolone 30 mg/day, treatment response was good including clinical symptoms, laboratory biomarker and chest imaging findings. She is well on prednisolone 2.5 mg/day now.

Discussion: This case show similar presentation of f-NSIP both clinically and radiologically. Multidisciplinary discussion was useful for decide to commence adequate management.

Conclusion: We present a fibrotic sarcoidosis patient who mimics f-NSIP.

Keywords: *Fibrotic; sarcoidosis; non-specific interstitial pneumonia; Krebs von den Lungen-6; granuloma.*

1. INTRODUCTION

Sarcoidosis is a systemic granulomatous disease involving eye, lymph nodes, lung, heart and skin [1]. Japanese sarcoidosis patients often show eye and heart symptoms such as blurred vision, chest pain, palpitation and syncope [2]. Pathogenesis of blurred vision is intraocular inflammation due to granuloma. In pulmonary sarcoidosis, African-American patients sometimes have fibrotic process [3]. However, Japanese sarcoidosis patients usually show asymptomatic bilateral hilar lymphadenopathy of chest imaging especially in young man [4,5]. On the other hand, Japanese elderly woman sometimes demonstrate symptomatic heart disease such as complete atrioventricular block or lung disease [6]. Pulmonary fibrotic sarcoidosis is unusual in Japan. We herein report a case of pulmonary fibrotic sarcoidosis patient who's clinical symptoms and chest imaging mimics fibrotic NSIP.

2. PRESENTATION OF CASE

A 75-year-old lady Japanese presented with fifteen months duration of non-productive cough and one month exertional dyspnea. Her medical history was hypertension only, and her family history including connective tissue disease (CTD) or interstitial lung disease (ILD) was unremarkable. She was never smoker. However her husband was active smoker. Her regular medication was anti-hypertensive drug and no other habitual drugs.

She noticed non-productive cough fifteen months ago. Her local doctor prescribed her anti-tussive, but her symptom did not improve. In addition, she developed exertional dyspnea, which

progressively worsened. Her modified medical research council (mMRC) breathlessness score was 2. Therefore, she was referred to our hospital. She denied blurred vision, dry eye, dry mouth, sputum, chest pain, palpitation, joint pain, muscle ache, rash, fever, appetite loss and body weight loss.

Findings on our outpatient service: blood pressure, 184/102 mmHg; heart rate, 106/beat per minute, regular; respiratory rate, 24/minute; body temperature, 35.6°C; and SpO₂, 95% (room air). General appearance was not in acute distress. Her palpebral conjunctiva was not anemic and bulbar conjunctiva was not icteric. Oral hygiene was good. Neck showed no lymphadenopathy. Bilateral fine crackles were audible at bilateral lung base and squawk was heard at left lung base. Wheezes was not heard. Neither heart murmur nor extra heart sound such as S3 or S4 were observed. There were no hepatosplenomegaly of note and no edema, finger clubbing, muscle pain, arthralgia and rash in extremities.

Laboratory findings on outpatient basis were elevation of LDH 323 IU/L and KL-6 4761 U/ml. Inflammation marker such as white blood cell (WBC) count and C-reactive protein (CRP) level were within the normal range. Creatine phosphokinase (CPK) was also negative. Urinalysis was normal. Autoimmune panel such as rheumatoid factor (RF), anti-nuclear antibody (ANA), anti aminoacyl tRNA synthetase (ARS) antibody, and myeloperoxidase anti-neutrophil cytoplasmic antibody (MPO-ANCA) were all negative. In terms of sarcoidosis marker, angiotensin converting enzyme (ACE) was negative and soluble interleukin 2 receptor (S-IL-2 R) was 686 U/ml.



Fig. 1. Initial chest radiograph revealed reticulo nodular shadow in bilateral lower lung field, volume loss and mediastinal fullness

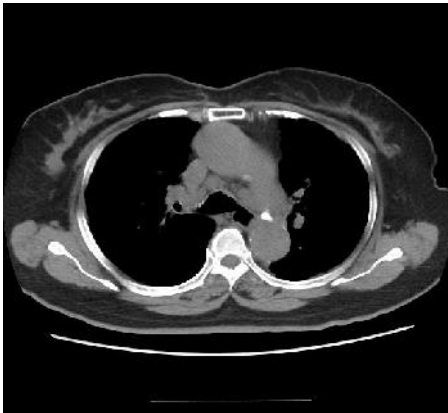
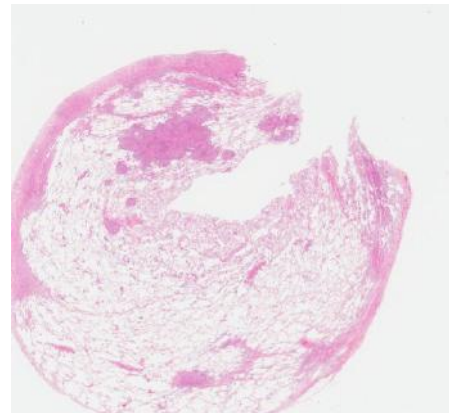


Fig. 2. (A) Initial chest CT mediastinal window showed lymphadenopathy



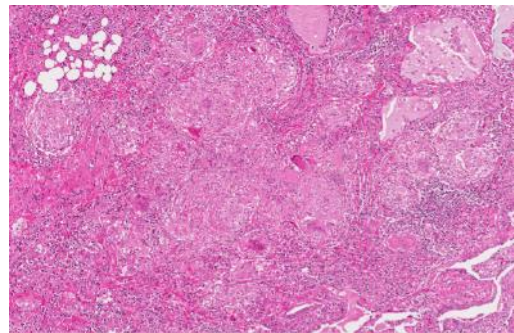
Fig. 2. (B) Initial chest CT lung window showed left lung predominant peri-bronchovascular consolidation, reticular shadow and traction bronchiectasis without honeycombing

Chest radiograph revealed reticulo nodular shadow in bilateral lower lung field, volume loss and mediastinal fullness. (Fig. 1) Chest HRCT showed mediastinal lymphadenopathy and left lung predominant peri-bronchovascular consolidation, reticular shadow and traction bronchiectasis without honeycombing (Fig. 2A-B).



Low power field H & E

Fig. 3. (A) Specimen from left S3 revealed peri-lymphatic granuloma

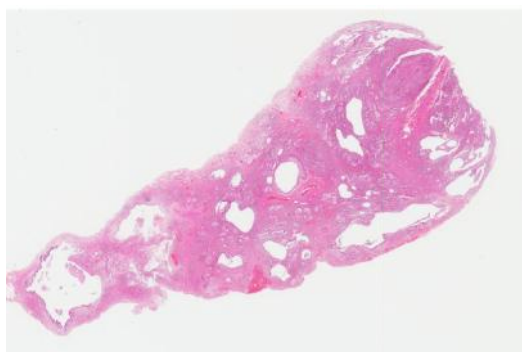


High power field H & E

Fig. 3. (B) Specimen from left S3 showed well formed granuloma

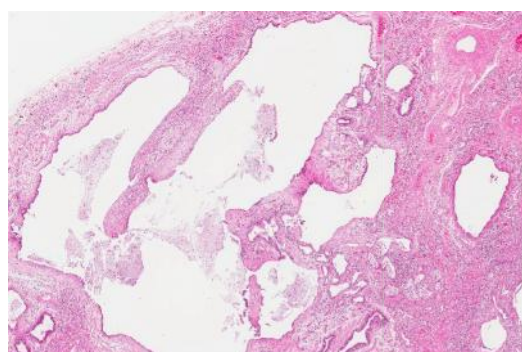
PFT showed severe restrictive disorder such as FVC 1.12 L and % FVC was 52.8%. Electrocardiogram (ECG) showed normal axis and no AV block. Based on this information, we suspected this case as f-NSIP because of lower lobe predominant fibrotic process without eye and heart symptoms. And we omit trans bronchial lung biopsy (TBLB) and broncho alveolar lavage (BAL) because we thought sufficient material will be required for definite

pathological diagnosis. She undertook VATS and two materials were taken from left S3 and S10. Pathological findings of S3 showed peri-lymphatic granuloma (Fig. 3A-B) and S10 revealed granuloma and dense fibrosis including microscopic honeycombing. (Fig. 4A-B) Tuberculin skin test was completely negative. And Galliumscan was negative. According to the clinical symptoms, radiological findings and pathological findings, our final diagnosis was pulmonary fibrotic sarcoidosis. We commenced oral prednisolone 30 mg/day with good clinical course. In laboratory findings serum KL-6 dramatically decreased from 4761 U/ml to 1083 U/ml within three months. And radiological findings also improved three months [and one year later. (Fig. 5) In addition, FVC increased from 1.12L to 1.23L over one year. Prednisolone dose was gradually tapered to 2.5 mg sixteen months later and she is doing well now.



Low power field H&E

Fig. 4. (A) Specimen from left S10 revealed dense fibrosis and granuloma



High power field H&E

Fig. 4. (B) Specimen from left S10 showed microscopic honeycombing

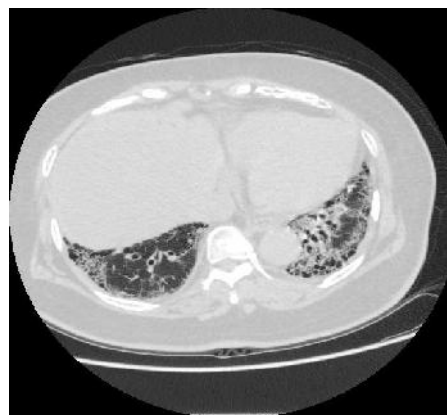


Fig. 5. Chest CT one year later after treatment

3. DISCUSSION

Our case showed lower lobe predominant reticular shadow, peri-bronchovascular consolidation and lower lung field volume loss. These imaging findings are rather consistent with anti-ARS syndrome [7,8]. In addition, exertional dyspnea progressed for one month with severe restrictive disorder based on PFT. Such subacute fibrotic lung disease, we usually consider organizing pneumonia (OP), f-NSIP, subacute hypersensitivity pneumonia (HP) and drug induced pneumonia. Clinical point of view, she had no apparent environment exposure and took no causative drug including supplement and herbal medicine. Regarding sarcoidosis, she had no eye symptoms such as blurred vision, dry eye and ECG showed normal findings [9]. Therefore, typical Japanese sarcoidosis presentation were absent. Most common sign and symptoms of Japanese typical sarcoidosis patient are neck lymphadenopathy, blurred vision and palpitation. In addition, her chest HRCT findings revealed no upper lung field predominance and granular shadow. Only consistent findings of sarcoidosis was mediastinal lymphadenopathy [10]. Based on these information, our most possible diagnosis before biopsy was f-NSIP or fibrosing organizing pneumonia (fOP) [11]. Pathological findings showed peri-lymphatic well formed granuloma, dense fibrosis and architectural destruction such as microscopic honeycombing especially lower lung field. According to the 2011 idiopathic pulmonary fibrosis (IPF) guideline, our case was not pathological usual interstitial pneumonia (UIP) [12]. Through clinical radiological pathological discussion, we arrived at pulmonary fibrotic sarcoidosis [13]. Other interesting findings was marked elevation of her serum KL-6. KL-6 is a high-molecular weight

protein and useful marker of fibrotic lung disease [14]. However, serum ACE is more often elevated in sarcoidosis patients [15,16]. With pathological findings, our case had repetitive extensive injury of alveolar type II cell and more fibrotic area than granuloma volume. This findings was accordance with negative findings of Ga scan [17]. In typical Japanese sarcoidosis patient, only bilateral hilum lymphadenopathy was seen without symptom. General indication of systemic prednisolone are cardiac, neurogenic and fibrotic sarcoidosis. After starting treatment based on definite diagnosis of fibrotic sarcoidosis,our case showed good response including clinical symptoms, laboratory data, PFT and radiological findings. However, pulmonary fibrotic sarcoidosis patients often show persistent symptoms and poor survival. Therefore,we should monitor this case carefully indefinitely because of poor pulmonary function and pathological dense fibrosis which suggest non-favorable prognosis.

4. CONCLUSION

We report a case of pulmonary fibrotic sarcoidosis patient who mimics f-NSIP. So, multi disciplinary discussion including physician, radiologist and pathologist is important for providing adequate management of atypical fibrotic lung disease.

CONSENT

All authors declared that informed consent was obtained from the patient for publication of this paper.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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